Environment International 92–93 (2016) 707–715

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Systematic review of differential inorganic arsenic exposure in minority, low-income, and indigenous populations in the United States

Lauren Joca [a], Jason D. Sacks [b], Danielle Moore [a], Janice S. Lee [c], Reeder Sams II [d], John Cowden [d]

[a] ORISE Fellow, Hazardous Pollutant Assessment Group, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
[b] Environmental Media Assessment Group, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
[c] Integrated Risk Information System Division, National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
[d] Hazardous Pollutant Assessment Group, National Center for Environmental Assessment, Research Triangle Park Division, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA

article info

Article history:
Received 30 March 2015
Received in revised form 30 November 2015
Accepted 13 January 2016
Available online 18 February 2016

Keywords:
Arsenic
Environmental justice
Systematic review
Differential exposure

abstract

Inorganic arsenic (iAs) is a human carcinogen and associated with cardiovascular, respiratory, and skin diseases. Natural and anthropogenic sources contribute to low concentrations of iAs in water, food, soil, and air. Differential exposure to environmental hazards in minority, indigenous, and low income populations is considered an environmental justice (EJ) concern, yet it is unclear if higher iAs exposure occurs in these populations. A systematic review was conducted to evaluate evidence for differential iAs exposure in the United States (US). The peer-reviewed literature was searched for studies that (1) estimated iAs exposure based on environmental concentrations of iAs in water, food, soil, or iAs biomarkers and (2) examined iAs exposure in minority, indigenous, and low income US populations. Five studies were identified that estimated exposures and provided demographic information about EJ populations. These studies reported arsenic concentrations in water, soil, or food to estimate exposure, with varied evidence of differential exposure. Additionally, six studies were identified that suggested potential arsenic exposure from environmental sources including soil, rice, private well-water, and fish, but did not report data stratified by demographic information. Evidence across these 11 studies was qualitatively integrated to draw conclusions about differential iAs exposure. The total body of evidence is limited by lack of individual exposure measures, lack of iAs concentration data, and insufficient comparative demographic data. Based upon these data gaps, there is inadequate evidence to conclude whether differential exposure to iAs is an EJ concern in the US.

Published by Elsevier Ltd.

1. Introduction

Exposure to inorganic arsenic (iAs) is associated with human health effects including skin, lung, bladder, renal, and hepatic cancers (Chen et al., 1992; Chen et al., 1988; Kurttio et al., 1999; Tsai et al., 1999; Yang et al., 2004; Yuan et al., 2007; Hunt et al., 2014; Tsuji et al., 2014a; Karagas et al., 2015; Roy et al., 2015), as well as non-cancer effects including diabetes mellitus, cardiovascular disease, and developmental effects (Calderon et al., 2001; Chang et al., 2004; Rahman et al., 1998; Tsai et al., 2003; Abhyankar et al., 2012; Tsuji et al., 2014b; Bailey et al., 2015; Davis et al., 2015; Farzan et al., 2015a; Farzan et al., 2015b; Kuo et al., 2015; Mendez et al., 2015; Sanders et al., 2014). Chronic exposure to high levels of iAs represents a global public health concern (Nahar et al., 2008; Naujokas et al., 2013; Huang et al., 2015). High concentrations of iAs in water systems (Anawar et al., 2002; Ghosh et al., 2008) in Bangladesh, China, Taiwan and India have resulted in numerous health effects including premalignant skin lesions (Argos et al., 2004; Argos et al., 2007; De Chaudhuri et al., 2006); blackfoot disease and other cardiovascular diseases (Chen and Wang, 1990), and a high incidence of cancer (Chiou et al., 1995; Su et al., 2010).

Based upon the health effects associated with iAs exposure, the US Environmental Protection Agency (US EPA) established a maximum contaminant level (MCL) of 10 μg/L arsenic (U.S. EPA, 2001). Compliance with the revised arsenic standard was required by 2006 and water consumption is only one route of exposure; therefore, certain populations may still experience exposures above the MCL. Increased risk of exposure to environmental hazards often occurs disproportionately in minority or low income populations, potentially representing an EJ concern. Guidance for assessing EJ concerns has been developed by the US EPA (U.S. EPA, 2013a). This technical guidance defines potential populations of concern as minority, low income, and indigenous populations and identifies differential exposures as a key consideration for developing human health risk assessments (U.S. EPA, 2013a).

It is unclear if differential iAs exposure represents an EJ concern within the US. To address this potential EJ concern, a systematic review was conducted to identify, evaluate, and characterize the available data on differential iAs exposure in low-income, minority, and indigenous populations within the US. Exposure in these specific populations was compared to exposure in groups not identified as population groups of

Corresponding author.
E-mail address: cowden.john@epa.gov (J. Cowden).

http://dx.doi.org/10.1016/j.envint.2016.01.011
0160-4120/Published by Elsevier Ltd.

concern in the US EPA's "Draft Technical Guidance for Assessing Environmental Justice in Regulatory Analysis" (U.S. EPA, 2013a). The characterization of the evidence across studies evaluated formed the basis of the conclusions reflecting the overall level of confidence with respect to whether specific populations of concern experience differential iAs exposure.

2. Methods

2.1. Literature search strategy

We conducted a systematic literature search to identify the available data on arsenic exposure and potential populations of concern. A study was eligible for inclusion if it examined arsenic exposure among low income, minority, or indigenous populations within the US. An initial search strategy was used to broadly capture literature related to arsenic. This general arsenic literature search accessed PubMed, Web of Science, and ToxNet databases on November 21, 2013 (Supplement 1). The literature search was periodically repeated through December 31, 2014.

Our review is focused on populations of concern as defined in the US EPA's "Draft Technical Guidance for Assessing Environmental Justice in Regulatory Analysis" (U.S. EPA, 2013a). Therefore, we constructed a list of search terms commonly used to describe low-income, minority, and indigenous populations (Supplement 2) to identify relevant literature. These terms were compiled from studies during preliminary analyses of EJ concerns in the US. We included studies with at least one of these terms in either the title, abstract, or medical subject headings (MeSH). This approach was intended to identify studies that examined the general adult population and stratified results by race, ethnicity, or socioeconomic status.

2.2. Study selection

To identify potentially relevant studies that focused on arsenic exposure in populations of concern we applied additional criteria to further

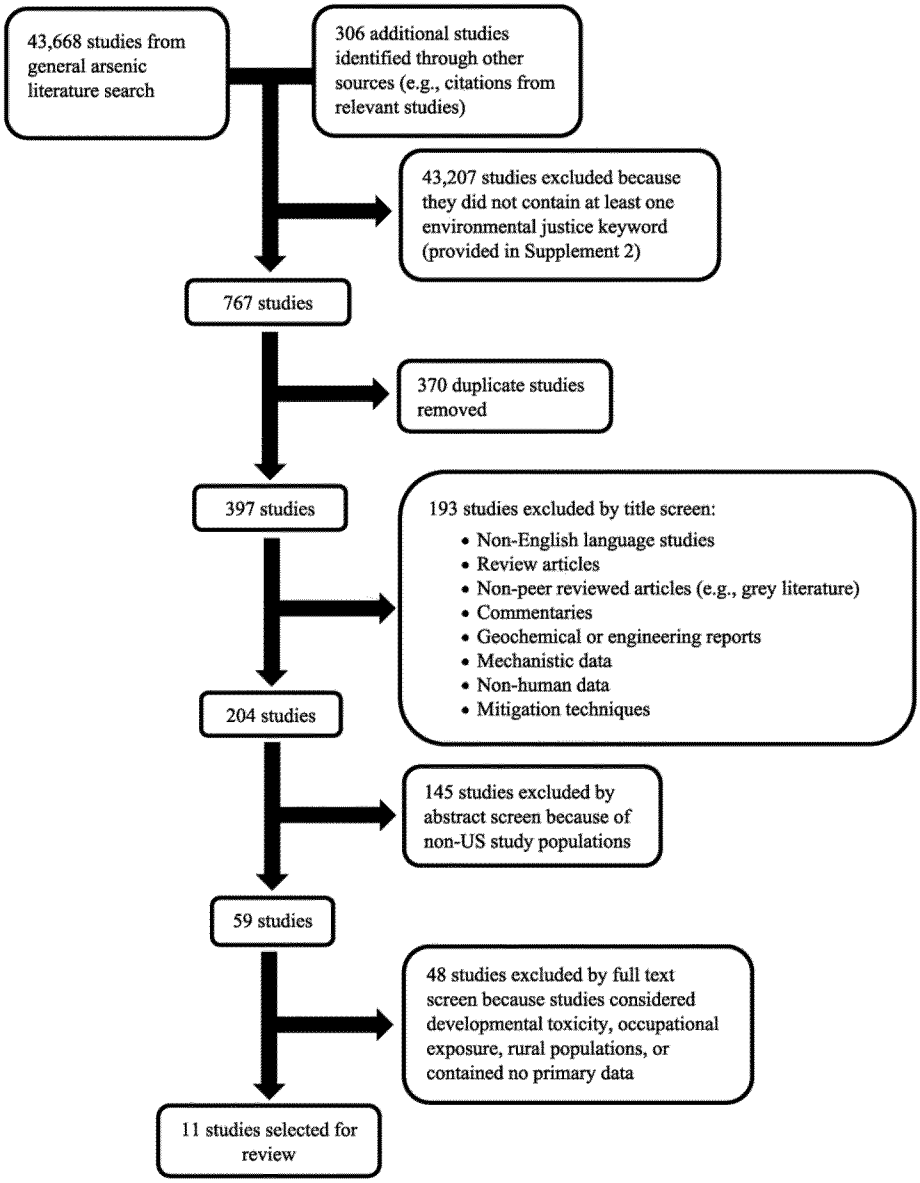

Fig. 1. Literature search flow diagram. Arsenic peer-reviewed studies containing key words for environmental justice in the title, abstract, or MeSH terms were screened for US populations and differential iAs exposure.

refine the literature search as detailed in Fig. 1. When the list of terms commonly used to describe low-income, minority, and indigenous populations (Supplement 2) was applied to these search results, 767 studies were identified; 397 unique studies remained once duplicate studies were removed. Title screening excluded 193 studies because they were non-English language studies, reviews, non-peer reviewed articles (e.g., gray literature), commentaries, or geochemical and engineering reports. At this stage, studies that focused on mechanistic data, non-human data, or mitigation technologies were also excluded from consideration using a title screen. A review of the abstracts removed another 145 studies that did not have study groups within the US. This screening process resulted in 59 studies. Both title and abstract screening were done independently by two reviewers.

At this point, studies were evaluated independently by two reviewers to identify studies for inclusion. Occupational and rural data that did not include socioeconomic or demographic information were excluded from consideration. Studies on differential iAs exposure in children were not considered because this analysis focused on potential differential exposure in populations of concern, rather than life stage susceptibility.

The final pool of 11 studies identified were peer-reviewed studies that included an internal or environmental measure of arsenic exposure and demographically or socioeconomically stratified results of a US population, allowing for comparison of exposures across populations within the same study design. This comparative approach is used by the U.S. EPA to characterize populations potentially at increased risk of air pollutant-related health effects and increased exposures as detailed in Vinikoor-Imler et al. (2014) and U.S. EPA (2013b). Based upon these criteria, 11 studies were identified that informed the potential for differential exposure to iAs across different populations of concern (Table 1).

2.3. Risk of bias evaluation for individual studies

The 11 studies identified in the literature search were evaluated for risk of bias. The risk of bias evaluations were performed using a modified approach based on the National Toxicology Program's Office of

Table 1
Summary of individual studies. Selected findings and data from the eleven identified studies are shown. Studies are arranged into three groups based upon inorganic arsenic (iAs) exposure measurements (direct or indirect) and demographic information. Within each group, the studies are presented alphabetically. Selected findings informed the evaluation of differential iAs exposure in populations of concern. DMA = dimethylarsinic acid; MCL = maximum contaminant level.

	Study	Study summary	Sample size	Measurement of iAs exposure	Exposure source	Demographic information
Direct iAs measures	Gilbert-Diamond et al. (2011)	Pregnancy cohort	229 women	Direct — urinary concentrations of iAs	Dietary	Not stratified by race or income
	Wei et al. (2013)	National Health and Nutrition Examination Study (NHANES); 2003–2006	3207 urine samples	Direct — urinary concentrations of iAs	Dietary	Stratified by race (Non-Hispanic white, Non-Hispanic black, Hispanic, or "Other" including Asian, other race and multi-racial) and income (b$35,000 or ≥$35,000)
Indirect iAs measures and limited demographic information	Balazs et al. (2012)	Study of Community Water Systems (CWS)	464 CWS serving 1,134,017 people	Indirect — arsenic MCL violations	Water	Stratified by race (Non-Hispanic whites or "People of color" including Latinos and non-Latinos), home ownership, and poverty level (above or below 200% of the U.S. poverty level)
	Diawara et al. (2006)	Geochemical study	33 Urban sites (66 soil samples)	Indirect — arsenic concentrations in topsoil	Soil	Stratified by race (White non-Hispanic, African American, or Hispanic) and socioeconomic status ("low income")
	Landolt et al. (1985)	Study of anglers in Puget Sound and contaminant concentrations in fish	4181 anglers interviewed, although ~25% were interviewed more than once	Indirect — arsenic concentration in fish tissue	Dietary	Stratified by race (Caucasian, Black, American Indian, Asian, Pacific Islander, Hispanic, or Other)
	O'Rourke et al. (1999)	National Human Exposure Assessment Survey (NHEXAS) — Arizona	175 individuals — 70 males and 105 females	Indirect — arsenic concentrations in air, soil, house dust, food, beverage, and water	Environmental media	Stratified by race (Hispanic or Non-Hispanic)
	Pellizzari et al. (1999)	NHEXAS — EPA Region V	326 individuals — 131 males and 195 females	Indirect — arsenic concentration in personal and environmental samples	Environmental media	Stratified by race and income (Non-minority or "Minority" consisting of White Hispanic, Black, and Others)
	Tyrrell et al. (2013)	NHANES — 2003–2010	17,405 urine samples	Indirect — arsenic measured in urine	Environmental media	Stratified by race (Mexican Hispanics, Non-Hispanic whites, and Non-Hispanic Blacks) and income (Poverty Index Ratio)
Indirect iAs measures and insufficient demographic analysis	Johnson et al. (2011)	Case–control analysis contaminant exposure in residents of 23 rural Appalachian Kentucky counties and urban Jefferson county	239 samples (169 samples below detection limit for arsenic)	Indirect — arsenic concentration in toenail samples	Environmental media	Stratified by race (White, Black, or other) and location (Urban or Rural)
	Postma et al. (2011)	Report of sample proportions from well water quality test in Intervention Study	188 households	Indirect — arsenic concentration in water samples	Water	Stratified by race (American Indian/Alaska Native, Asian, Black or African American, White, Other, or Multi-racial) and income (≥$24,999, $25,000–$49,999, or ≥$50,000)
	Walker et al. (2005)	Survey and exposure study	351 households	Indirect — arsenic concentration in water samples	Water	Income information collected but not presented in study

Health Assessment and Translation (OHAT) method for conducting literature-based evidence assessments (Rooney et al., 2014). The OHAT approach uses 15 questions to evaluate selection bias, confounding bias, performance bias, attrition/exclusion bias, detection bias, selective reporting bias, and internal validity. Because our systematic review focused on human exposure data and our literature search did not find any controlled human exposure studies, we did not evaluate risk of bias using the OHAT questions for experimental animal or controlled human exposure studies. We also did not evaluation confounding bias because our review is focused only on exposure and confounders impact both exposure and effect. The remaining 8 OHAT questions used to evaluate risk of bias and specific criteria for evaluating each risk of bias question are shown in Supplement 3.

To evaluate risk of bias, two reviewers independently evaluated each study and determined ratings (i.e., + + : definitely low risk of bias, + : probably low risk of bias, − : probably high risk of bias, or − − : definitely high risk of bias) for a series questions. The two reviewers discussed and resolved any differences in ratings entered for a particular OHAT question. A summary of the risk of bias evaluations for each study is shown in Table 2. The rationale for each risk of bias rating is detailed in Supplement 4. The risk of bias evaluation did not eliminate studies from consideration; rather, the ratings of each individual study were considered during overall evaluation of the evidence.

2.4. Extraction of study data

To facilitate comparative analyses, study information was organized into a summary evidence table that included study design, measures of iAs, and selected results (Table 1). This table was developed by one person and independently reviewed by two reviewers. Study design information extracted included the outcome measures and the statistical and/or chemical analyses. The data extracted from each study included arsenic measurement methods and demographic information reported. For measures of arsenic exposure, Table 1 indicates direct or indirect iAs exposure measurements and, if available, if the measurements were found in biomarkers such as urine, toenails, or hair. For environmental exposure studies, the results extracted from the studies included levels of inorganic arsenic in water and soil. Where available, demographic characteristics were recorded.

Table 2
Summary of risk of bias evaluations for individual studies. For the eleven studies identified, a risk of bias evaluation was made for each risk of bias question. + + = definitely low risk of bias (green); + = probably low risk of bias (light green); − = probably high risk of bias (light red); − − = definitely high risk of bias (red).

Bias category	Question(s)	Gilbert–Diamond et al. (2011)	Wei et al. (2014)	Balazs et al. (2012)	Diawara et al. (2006)	Landolt et al. (1985)	O'Rourke et al. (1999)	Pellizzari et al. (1999)	Tyrrell et al. (2013)	Johnson et al. (2011)	Postma et al. (2011)	Walker et al. (2005)
Selection bias	Were the comparison groups appropriate?	++	++	–	–	–	+	+	++	–	–	+
Performance bias	Did deviations from the study protocol impact the results?	++	++	+	++	+	++	++	+	++	++	++
Attrition/ exclusion bias	Were demographic data incomplete due to attrition or exclusion from analysis?	++	+	++	+	++	+	++	++	+	++	++
Detection bias	Were the outcome assessors blinded to study group or exposure levels?	+	+	+	+	+	+	+	+	+	+	+
	Did researchers adjust or control for other exposures that are anticipated to bias results?	++	+	+	++	—	+	++	–	–	–	–
	Can we be confident in the exposure characterization?	+	—	—	—	—	+	+	—	—	Not applicable	—
	Can we be confident in the outcome assessment?	+	+	+	–	–	++	++	+	–	—	++
Selective reporting bias	Were all measured demographics reported?	++	++	+	+	++	++	+	+	++	++	–

Extracted data were used to group the studies for consideration. If a study specifically reported iAs concentrations, we refer to the findings as "iAs." If a study did not report iAs concentrations, we refer to the exposure as "arsenic." Studies with direct measures of iAs exposure in humans and comparative demographics information were considered the most informative for our analysis. Studies with indirect measurements of human iAs exposure (e.g., environmental measures) and comparative demographics information, or studies with direct measures of human iAs exposure but limited comparative demographic information, provided supportive information for our analysis. Studies with indirect measurements of human iAs exposure and insufficient comparative demographic information were considered the least informative studies for our analysis.

2.5. Characterization of evidence

The body of evidence was characterized to determine overall confidence that a specific population had a greater risk of increased iAs exposure using an approach based on the causal framework developed the U.S. EPA (U.S. EPA, 2013b; Vinikoor-Imler et al., 2014). This modified framework was used to determine whether evidence of increased risk of differential iAs exposure in populations of concern (i.e., minority, low-income, or indigenous populations) is adequate, suggestive, inadequate, or whether there is evidence of no effect (Table 3). During the characterization of the evidence, consistency across studies was an important consideration, specifically with respect to the measures of iAs exposure. Importantly, this modified approach is not a checklist, but rather an integrative approach using systematic evaluations and scientific judgment to draw conclusions based upon the available evidence.

3. Results

3.1. Summary of studies

The study characteristics considered relevant for this review, particularly methods to estimate iAs exposure and demographic information, are summarized in Table 1. Of the eleven studies, three considered iAs exposure through drinking water, one considered soil exclusively, and three estimated dietary exposures to arsenic. One study examined fish and subsistence fishing as possible routes of arsenic exposure. Finally, three studies used a composite metric of arsenic exposure. Of the three studies examining aggregate exposure, two studies used National Human Exposure Assessment Survey (NHEXAS) data on arsenic measures from water, soil, and personal air.

Table 3
Classification of evidence. The body of evidence was integrated to determine if data for differential iAs exposure in populations of concern were adequate, suggestive, inadequate, or evidence of no effect. Criteria for each level were developed for this review.

Adequate evidence	There is substantial, consistent evidence to conclude that minority, low-income, or indigenous populations are exposed to higher levels of iAs relative to other populations. Evidence includes consistency across multiple, high-quality studies that include direct measures of iAs exposure, either in media or through biomarker data, as well as sufficient demographic information to allow comparisons between relevant populations.
Suggestive evidence	The collective evidence suggests minority, low-income, or indigenous populations are exposed to higher levels of iAs relative to other populations, but the evidence is limited due to inconsistency, indirect measures of iAs exposure, and demographic information that allows only limited comparisons between relevant populations.
Inadequate evidence	The collective evidence is inadequate to determine minority, low-income, or indigenous populations are exposed to higher levels of iAs relative to other populations. The available studies are of insufficient quantity, quality, consistency and/or statistical power to permit a conclusion to be drawn.
Evidence of no effect	There is substantial, consistent evidence minority, low-income, or indigenous populations are not exposed to higher levels of iAs relative to other populations. Evidence would include consistency across multiple, high-quality studies that include direct measures of iAs exposure, either in media or through biomarker data, as well as sufficient demographic information to allow comparisons between relevant populations.

3.1.1. Studies with direct iAs human exposure measures

Two studies reported direct measures of human iAs exposure. A study analyzing US National Health and Nutrition Examination Survey (NHANES) data reported differences in rice consumption and urine levels of iAs among "other" ethnic groups, including Asian and Pacific Islander, supporting dietary exposures as a source of differential iAs exposure (Wei et al., 2013). Similarly, a study of pregnant women in New Hampshire that examined urinary iAs levels reported that rice consumption increased urinary iAs concentration (Gilbert-Diamond et al., 2011). Although these authors did not stratify their data with demographic information, rice consumption surveys have shown that minorities and indigenous populations consume more rice than non-Hispanic whites (Batres-Marquez et al., 2009; Cleland et al., 2009), suggesting differential iAs exposure from rice consumption.

3.1.2. Studies with indirect iAs human exposure measures and demographic information

Several studies stratified arsenic exposure using demographic information (Balazs et al., 2012; Diawara et al., 2006; Landolt et al., 1985; O'Rourke et al., 1999; Pellizzari et al., 1999). Rather than measuring individual exposures, these studies estimated individual exposure using measures of arsenic in water, soil, or food. These studies did not provide iAs measurements; therefore, the exposure measurements were considered indirect measures of iAs exposure. Despite the exposure measure limitations, these studies provide informative data on potential differential iAs exposure in populations of concern. One study reported that low income populations in the San Joaquin Valley of California were more likely to be served by community water systems with higher arsenic levels and a greater likelihood of MCL violations (Balazs et al., 2012). In another study, the highest arsenic concentrations were found in a low socioeconomic community in Pueblo, Colorado; however, no statistical relationship was found between topsoil arsenic concentrations and ethnicity or household income (Diawara et al., 2006). Similarly, NHEXAS data did not find any relationship between increased arsenic concentrations in several different environmental media and ethnicity or income in Arizona (O'Rourke et al., 1999) and the Great Lakes Region (Pellizzari et al., 1999). In a study measuring arsenic concentrations in recreationally caught fish species in the Puget Sound, Landolt et al. (1985) observed no statistical relationship between ethnicity and consumption of fish with higher arsenic concentrations.

One study examined the impact of socioeconomic status (SES) on exposure using indirect measures of iAs in individuals. Tyrrell et al. (2013) used urine measures taken for the NHANES as metrics of arsenic exposure. The authors used linear regression between the biomonitoring exposure data and the poverty index ratio (PIR) to determine the relationship between arsenic exposure and SES. Using over 7 years of NHANES data (from 2003 to 2010), the authors found an inverse relationship between PIR and arsenic exposure, indicating that individuals with higher SES had higher arsenic exposure. While this finding suggests populations of concern may not experience higher levels of exposure, a limitation of this study was use of total arsenic as the exposure metric. Total arsenic measures both iAs and organic arsenic. Unlike iAs, organic arsenic is considered relatively non-toxic (ATSDR, 2007). Organic arsenic exposure can occur through consumption of seafood (Health Canada, 2006) and Tyrell et al. reported that fish and shellfish consumption were mediators in the relationship between PIR and arsenic exposure (Tyrrell et al., 2013). Therefore, the inverse relationship between SES and total arsenic exposure may reflect dietary differences

between populations, with higher seafood consumption leading to increased total arsenic concentrations in higher SES populations.

3.1.3. Studies with indirect iAs exposure measures and limited demographic information

Other studies also suggest the potential for differential iAs exposure through private water supplies, but report measures of indirect iAs exposure with limited or no demographic data. Private domestic wells are not subject to management requirements set by the Safe Water Drinking Act, potentially leading to increased toxicant exposure in populations using well-water for consumption. While several studies reported higher arsenic concentrations and exposure associated with domestic well-water consumption in rural populations throughout the US (Johnson et al., 2011; Postma et al., 2011; Walker et al., 2005), these studies lack information on ethnic or socioeconomic factors to indicate differential exposure in populations of concern.

3.2. Risk of bias evaluation for individual studies

Risk of bias evaluations revealed that the studies did not deviate from the planned protocols and did not produce incomplete data due to attrition or exclusion (Table 2). The study investigators were appropriately blinded to exposure levels and the studies did not show selective bias in reporting demographic information. There were, however, some data gaps that limited the ability of these studies to inform potential for differential iAs exposure in populations of concern.

The identified studies generally did not provide information on the general population or other populations not defined as populations of concern within the study to compare with iAs exposure in populations of concern. Detection bias was present because of limitations in characterization of exposure. The studies generally did not report specific iAs concentrations or did not demonstrate direct exposure to iAs. Several studies did not control for potential bias from co-exposures to other environmental contaminants. These limitations reduced confidence in the exposure characterization and the ability to investigate the relationship between iAs exposure and demographic information.

3.3. Evidence integration

To evaluate the available evidence for differential iAs exposure in minority, low-income, or indigenous populations, we used an approach based upon the causal framework developed by the U.S. EPA for characterizing populations potentially at increased risk of an environmental chemical exposure (U.S. EPA, 2013b; Vinikoor-Imler et al., 2014). Table 3 describes the specific criteria for determining the overall confidence that populations of concern are at increased risk of higher iAs exposure. Two key features of this evidence integration framework include consistency across multiple studies with direct measures of iAs and sufficient demographic information to allow comparisons between relevant populations. Therefore, the available studies were grouped based upon iAs exposure and demographic as an initial step in evidence integration. Studies with indirect iAs measures and insufficient demographic information (Johnson et al., 2011; Postma et al., 2011; Walker et al., 2005) lacked sufficient data to inform differential iAs exposure in populations of concern and were not considered for evidence integration. The remaining eight studies were evaluated for evidence of differential iAs exposure in populations of concern.

Studies with both direct measures of iAs and sufficient information to allow comparisons between demographic groups were considered most informative. Of the studies we identified, only the NHANES study measured urinary concentrations of iAs and stratified exposure data by race and income (Wei et al., 2013). The authors reported that rice consumption was higher in minority populations and was subsequently associated with increased urinary total arsenic concentrations. The authors did not analyze the relationship between rice consumption and urinary iAs concentrations. Therefore, this study provides limited evidence of differential iAs exposure in minority populations.

Studies with direct or indirect measures of iAs exposure and limited comparative demographic information were considered for evidence of differential iAs exposure in populations of concern. One study reported that rice consumption was associated with higher urinary iAs concentrations (Gilbert-Diamond et al., 2011), but did not provide demographics information. The remaining studies reported indirect measures of iAs exposure, either through measuring arsenic in environmental samples (Balazs et al., 2012; Diawara et al., 2006; Landolt et al., 1985; O'Rourke et al., 1999; Pellizzari et al., 1999) or in urine (Tyrrell et al., 2013). One study reported a direct relationship between income and arsenic exposure (Tyrrell et al., 2013), although this observation may reflect differences in organic arsenic exposure from increased seafood consumption at higher income levels. Two studies did not observe associations between arsenic exposure in environmental samples and ethnicity or income (Balazs et al., 2012; Diawara et al., 2006; Landolt et al., 1985; O'Rourke et al., 1999; Pellizzari et al., 1999), while three studies suggested increased potential for arsenic exposure in minority populations (Balazs et al., 2012; Diawara et al., 2006; Landolt et al., 1985; O'Rourke et al., 1999; Pellizzari et al., 1999). Overall, these studies suggest that minorities have the potential for higher iAs exposures, either through drinking water violations or dietary differences; however, none of these studies provide direct evidence of increased iAs exposure in populations of concern.

As a final step in evidence integration, risk of bias evaluations were considered (Table 2, Supplement 4). Overall, the data are limited by exposure characterization, specifically the lack of individual exposure measures and measures of iAs. Although these studies used techniques that could distinguish inorganic arsenic and methylated arsenic species, the studies report measures of arsenic rather than iAs. The reviewed studies did not report any relationships between ethnicity or SES and iAs concentrations in various environmental media; however, the studies often lacked appropriate comparison groups, limiting the ability to determine differential exposures in populations of concern. Based on the modified integration framework (Table 3), the limited availability of data with direct iAs exposure and comparative demographic information, coupled with exposure characterization limitations of studies with indirect measures of iAs suggest there is inadequate evidence to determine whether populations of concern are at increased risk of differential iAs exposure.

4. Discussion

4.1. Summary of evidence

Our literature search identified eleven studies that were reviewed for informing the potential for differential iAs exposure in populations of concern. Of these eleven studies, eight had direct or indirect measures of iAs exposure and demographic information informing differential exposures. Risk of bias evaluations indicated that exposure characterization was a limitation of the reviewed literature.

The most consistent evidence of differential iAs exposure in populations of concern from dietary consumption of rice. Studies have reported a direct relationship between rice consumption and urinary iAs concentration (Gilbert-Diamond et al., 2011; Wei et al., 2013). Rice intake has been shown to vary based upon ethnicity, with minority populations consuming more rice (Batres-Marquez et al., 2009; Cleland et al., 2009; Hu et al., 2012). Dietary arsenic is a greater contributor to overall arsenic exposure than tap water consumption in certain populations (Thomas et al., 1999); therefore, dietary differences could contribute to differential iAs exposures across populations.

The evidence suggests that iAs in drinking water may be another source of differential exposure in populations of concern. The data demonstrate that low SES populations are more likely to use water systems in violation of the MCL (Balazs et al., 2012). In addition, several studies

have reported higher arsenic levels for populations using private, unregulated wells for drinking water consumption (Johnson et al., 2011; Postma et al., 2011; Walker et al., 2005). These studies define populations as "rural" or "urban" rather than providing ethnicity or socioeconomic information necessary to identify populations of concern. These studies also use environmental concentrations of arsenic to estimate exposure, rather than directly measuring iAs levels in individuals, limiting the ability to inform differences in iAs exposure from drinking water.

4.2. Limitations of the systematic review

The conclusions of this systematic review are based upon the studies identified using the outlined search strategy. Although broad search terms for EJ were established for inclusion, the a priori literature search criteria identified a limited the number of studies; therefore, the conclusions may be based on incomplete data. For example, data from Fallon, Nevada stratifying results according to socioeconomic variables was not collected in our original sample (Steinmaus et al., 2003). Similarly, arsenic exposure data collected as part of the San Luis Valley Diabetes Study (James et al., 2013) and Tar Creek Superfund Site studies (Ettinger et al., 2009) were not identified in the literature screen. These studies were missed was because the title, abstract, or MeSH terms did not contain a term on the environmental justice keyword list (Supplement 2). In addition, searching using broad EJ criteria rather than by specific ethnic group may also have missed relevant data and the effect of excluding non-peer reviewed literature (i.e., gray literature) is unknown. The challenges of developing a priori literature search criteria and drawing conclusions based a limited number of identified studies are important considerations when adopting systematic review methods for risk assessment. For systematic reviews of environmental contaminants, an iterative search strategy may ensure identification and review of all relevant literature.

The definition of populations of concern were based upon the US EPA's "Draft Technical Guidance for Assessing Environmental Justice in Regulatory Analysis" (U.S. EPA, 2013a), focusing the search to studies on low-income, minority, or indigenous populations. Other populations of interest for EJ concerns (Gochfeld and Burger, 2011) could include groups with occupational exposure, rural populations, and children. There is evidence that these populations face differential exposure to arsenic (Gochfeld and Burger, 2011; Knobeloch et al., 2013; Quandt et al., 2010; Sanders et al., 2012; Takahashi et al., 1983). For example, in Wisconsin, 940,000 rural households utilize private well water and 2.4% of the water supply contained concentrations of above the MCL (Knobeloch et al., 2013). Sanders et al., 2012, performed a spatiotemporal study examining iAs trends in private wells in North Carolina over an 11-year period and found that 2.25% of wells exceeded the MCL. These data suggest that rural counties are at increased risk of higher exposures due to a large proportion of the population relying on private wells (Sanders et al., 2012). Occupational exposures in the US also suggest potential higher levels of iAs exposure. Average urinary arsenic concentrations exceeded NHANES references values in farm workers (Quandt et al., 2010). Similarly, significantly higher mean arsenic levels were reported in wood treaters compared to the non-exposed group (Takahashi et al., 1983). Children are already treated as a population with increased risk to arsenic (U.S. EPA, 2005). It is possible that children within populations of concern are exposed at even greater levels than other children based on where they live, the employment of their parents, and the type of food and water they are drinking (Gochfeld and Burger, 2011; Vogt et al., 2012).

In the evaluated literature, exposure characterization is a limitation. Because total arsenic consists of both organic arsenic and iAs, it is difficult to draw conclusions on differential iAs exposure when studies report arsenic measurements rather than iAs specifically. In addition, most of the studies examined arsenic exposure from environmental media rather than individual biomarkers, further limiting conclusions on iAs exposure. The lack of adequate comparative demographics information also limits conclusions on differential iAs exposure in minority, low-income, or indigenous populations within the US.

4.3. Conclusions

This review used systematic approaches to evaluate literature on differential iAs exposure in minority, low-income, or indigenous populations within the US. The use of risk of bias methods and an evidence integration framework improved transparency of the conclusions. Selecting a priori literature search criteria, combined with non-iterative methods of identifying literature may have resulted in studies not being considered. Ensuring comprehensive literature identification would increase confidence in the conclusions of a systematic review.

This systematic review found limited data on iAs exposure in populations of concern. Elevated environmental levels of iAs in water and differential dietary exposures suggest a potential for greater iAs exposure in the populations of concern; however, the reviewed literature lacked iAs concentration data, information on individual exposures, and sufficient comparative demographic information. Because of limited number of studies identified, as well as limitations in the study reporting, there is inadequate evidence to determine whether populations of concern experience differential exposure to iAs within the US.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2016.01.011

Funding

This research was supported in part by an appointment to the Research Participation Program for the U.S. Environmental Protection Agency, Office of Research and Development, administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and EPA.

Competing financial interest declaration

The authors have no actual or potential competing financial interests.

Authors' contributions to manuscript

Literature search — Joca, Moore

Study review and data extraction — Joca, Cowden, Sacks

Evidence integration — Joca, Cowden, Sacks

Manuscript drafting/reviewing/editing — Joca, Lee, Cowden, Sacks, Sams

Disclaimer

The views expressed in this manuscript are those of the authors and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.

Acknowledgments

The authors gratefully acknowledge Dr. Tom Luben, Dr. Tim Wade, Dr. Lyle Burgoon, and Dr. John Vandenberg for their thoughtful review and insightful comments during manuscript preparation. The authors also gratefully acknowledge the guidance and insights provided by Dr. Andrew Rooney on the OHAT risk of bias approach.

References

Abhyankar, L.N., Jones, M.R., Guallar, E., Navas-Acien, A., 2012. Arsenic exposure and hypertension: a systematic review. Environ. Health Perspect. 120 (4), 494–500.

Anawar, H.M., Akai, J., Mostofa, K.M., Safiullah, S., Tareq, S.M., 2002. Arsenic poisoning in groundwater: health risk and geochemical sources in Bangladesh. Environ. Int. 27, 597–604.

Argos, M., Ahsan, H., Parvez, F., Chen, Y., Hussain, I., Momotaj, H., et al., 2004. The association between arsenic exposure and premalignant skin lesions is modified by socioeconomic status in a Bangladeshi population. Am. J. Epidemiol. 159, S21-S21.

Argos, M., Parvez, F., Chen, Y., Hussain, A.Z., Momotaj, H., Howe, G.R., et al., 2007. Socioeconomic status and risk for arsenic-related skin lesions in Bangladesh. Am. J. Public Health 97, 825–831.

ATSDR (Agency for Toxic Substances and Disease Registry), 2007. Toxicological Profile for Arsenic. Atlanta, GA.

Bailey, K.A., Smith, A.H., Tokar, E.J., Graziano, J.H., Kim, K.W., Navasumrit, P., et al., 2015. Mechanisms underlying latent disease risk associated with early-life arsenic exposure: current research trends and scientific gaps. Environ. Health Perspect. (2015 Jun 26 [Epub ahead of print]).

Balazs, C.L., Morello-Frosch, R., Hubbard, A., Ray, I., 2012. Environmental justice implications of arsenic contamination: a cross-sectional, cluster-design examining exposure and compliance in community drinking water systems. Environ. Heal.

Batres-Marquez, S.P., Jensen, H.H., Upton, J., 2009. Rice consumption in the United States: recent evidence from food consumption surveys. J. Am. Diet. Assoc. 109, 1719–1727.

Calderon, J., Navarro, M.E., Jimenez-Capdeville, M.E., Santos-Diaz, M.A., Golden, A., Rodriguez-Leyva, I., et al., 2001. Exposure to arsenic and lead and neuropsychological development in Mexican children. Environ. Res. 85, 69–76.

Chang, C.C., Ho, S.C., Tsai, S.S., Yang, C.Y., 2004. Ischemic heart disease mortality reduction in an arseniasis-endemic area in southwestern Taiwan after a switch in the tap-water supply system. J. Toxic. Environ. Health A 67, 1353–1361.

Chen, C.J., Wang, C.J., 1990. Ecological correlation between arsenic level in well water and age-adjusted mortality from malignant neoplasms. Cancer Res. 50, 5470–5474.

Chen, C.J., Kuo, T.L., Wu, M.M., 1988. Arsenic and cancers. Lancet 1, 414–415.

Chen, C., Chen, C., Wu, M., Kuo, T., 1992. Cancer potential in liver, lung, bladder and kidney due to ingested inorganic arsenic in drinking water. Br. J. Cancer 66, 888.

Chiou, H.Y., Hsueh, Y.M., Liaw, K.F., Horng, S.F., Chiang, M.H., Pa, Y.S., et al., 1995. Incidence of internal cancers and ingested inorganic arsenic — a 7-year follow-up study in Taiwan. Cancer Res. 55, 1296–1300.

Cleland, B., Tsuchiya, A., Kalman, D.A., Dills, R., Burbacher, T.M., White, J.W., et al., 2009. Arsenic exposure within the Korean community (United States) based on dietary behavior and arsenic levels in hair, urine, air, and water. Environ. Health Perspect. 117, 632–638.

Davis, M.A., Higgins, J., Li, Z., Gilbert-Diamond, D., Baker, E.R., Das, A., et al., 2015. Preliminary analysis of in utero low-level arsenic exposure and fetal growth using biometric measurements extracted from fetal ultrasound reports. Environ. Heal. 14, 12.

De Chaudhuri, S., Mahata, J., Das, J.K., Mukherjee, A., Ghosh, P., Sau, T.J., et al., 2006. Association of specific p53 polymorphisms with keratosis in individuals exposed to arsenic through drinking water in West Bengal, India. Mutat. Res. Fundam. Mol. Mech. Mutagen. 601, 102–112.

Diawara, M.M., Litt, J.S., Unis, D., Alfonso, N., Martinez, L., Crock, J.G., et al., 2006. Arsenic, cadmium, lead, and mercury in surface soils, pueblo, Colorado: implications for population health risk. Environ. Geochem. Health 28, 297–315.

Ettinger, A.S., Zota, A.R., Amarasiriwardena, C.J., Hopkins, M.R., Schwartz, J., Hu, H., et al., 2009. Maternal arsenic exposure and impaired glucose tolerance during pregnancy. Environ. Health Perspect. 117 (7), 1059–1064.

Farzan, S.F., Karagas, M.R., Jiang, J., Wu, F., Liu, M., Newman, J.D., et al., 2015a. Gene-arsenic interaction in longitudinal changes of blood pressure: findings from the Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh. Toxicol. Appl. Pharmacol. 288 (1), 95–105.

Farzan, S.F., Chen, Y., Rees, J.R., Zens, M.S., Karagas, M.R., 2015b. Risk of death from cardiovascular disease associated with low-level arsenic exposure among long-term smokers in a US population-based study. Toxicol. Appl. Pharmacol. 287 (2), 93–97.

Ghosh, P., Roy, C., Das, N.K., Sengupta, S.R., 2008. Epidemiology and prevention of chronic arsenicosis: an Indian perspective. Indian J. Dermatol. Venereol. Leprol. 74, 582–593.

Gilbert-Diamond, D., Cottingham, K.L., Gruber, J.F., Punshon, T., Vicki, S., Gandolfi, A.J., et al., 2011. Rice consumption contributes to arsenic exposure in US women. Proc. Natl. Acad. Sci. 108, 5.

Gochfeld, M., Burger, J., 2011. Disproportionate exposures in environmental justice and other populations: the importance of outliers. Am. J. Public Health 101 (Suppl. 1), S53–S63.

Health Canada, 2006. Guidelines for Canadian Drinking Water Quality: Guideline Technical Document — Arsenic. Water Quality and Health Bureau, Healthy Environments and Consumer Safety Branch, Health Canada, Ottawa, Ontario.

Hu, E.A., Pan, A., Malik, V., Sun, Q., 2012. White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review. BMJ 344.

Huang, L., Wu, H., van der Kuijp, T.J., 2015. The health effects of exposure to arsenic-contaminated drinking water: a review by global geographical distribution. Int. J. Environ. Health Res. 25 (4), 432–452.

Hunt, K.M., Srivastava, R.K., Elmets, C.A., Athar, M., 2014. The mechanistic basis of arsenicosis: pathogenesis of skin cancer. Cancer Lett. 354 (2), 211–219.

James, K.A., Marshall, J.A., Hokanson, J.E., Meliker, J.R., Zerbe, G.O., Byers, T.E., 2013. A case-cohort study examining lifetime exposure to inorganic arsenic in drinking water and diabetes mellitus. Environ. Res. 123, 33–38.

Johnson, N., Shelton, B.J., Hopenhayn, C., Tucker, T.T., Unrine, J.M., et al., 2011. Concentrations of arsenic, chromium, and nickel in toenail samples from Appalachian Kentucky residents. J. Environ. Pathol. Toxicol. Oncol. 30, 11.

Karagas, M.R., Gossai, A., Pierce, B., Ahsan, H., 2015. Drinking water arsenic contamination, skin lesions, and malignancies: a systematic review of the global evidence. Curr. Environ. Health Rep. 2 (1), 52–68.

Knobeloch, L., Gorski, P., Christenson, M., Anderson, H., 2013. Private drinking water quality in rural Wisconsin. J. Environ. Health 75, 16–20.

Kuo, C.C., Howard, B.V., Umans, J.G., Gribble, M.O., Best, L.G., Francesconi, K.A., et al., 2015. Arsenic exposure, arsenic metabolism, and incident diabetes in the strong heart study. 38 (4), 620–627.

Kurttio, P., Pukkala, E., Kahelin, H., Auvinen, A., Pekkanen, J., 1999. Arsenic concentrations in well water and risk of bladder and kidney cancer in Finland. Environ. Health Perspect. 107, 705–710.

Landolt, M.L., Hafer, F.R., Nevissi, A., Van Belle, G., Van Ness, K., Rockwell, C., 1985. Potential Toxicant Exposure Among Consumers of Recreationally Caught Fish from Urban Embayments of Puget Sound. EPIDEM/001132. National Oceanic and Atmospheric Administration.

Mendez, M.A., Gonzalez-Horta, C., Sanchez-Ramirez, B., Ballinas-Casarrubias, L., Hernandez Ceron, R., Viniegra Morales, D., et al., 2015. Chronic exposure to arsenic and markers of cardiometabolic risk — a cross-sectional study in Chihuahua, Mexico. Environ. Health Perspect. (Jun 12 [Epub ahead of print]).

Nahar, N., Hossain, F., Hossain, M.D., 2008. Health and socioeconomic effects of groundwater arsenic contamination in rural Bangladesh: new evidence from field surveys. J. Environ. Health 70, 6.

Naujokas, M.F., Anderson, B., Ahsan, H., Aposhian, H.V., Graziano, J.H., Thompson, C., 2013. He broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. Environ. Health Perspect. 121 (3), 295–302.

O'Rourke, M.K., van de Water, P.K., Jin, S., Rogan, S.P., Weiss, A.D., Gordon, S.M., et al., 1999. Evaluations of primary metals from NHEXAS Arizona: distributions and preliminary exposures. National Human Exposure Assessment Survey. J. Expo. Anal. Environ. Epidemiol. 9, 435–445.

Pellizzari, E.D., Perritt, R.L., Clayton, C.A., 1999. National human exposure assessment survey (NHEXAS): exploratory survey of exposure among population subgroups in EPA region V. J. Expo. Sci. Environ. Epidemiol. 9, 49–55.

Postma, J., Butterfield, P.W., Odom-Maryon, T., Hill, W., Butterfield, P.G., 2011. Rural children's exposure to well water contaminants: implications in light of the American academy of pediatrics' recent policy statement. J. Am. Acad. Nurse Pract. 23, 258–265.

Quandt, S.A., Jones, B.T., Talton, J.W., Whalley, L.E., Galvan, L., Vallejos, Q.M., et al., 2010. Heavy metals exposures among Mexican farmworkers in eastern North Carolina. Environ. Res. 110, 83–88.

Rahman, M., Tondel, M., Ahmad, S.A., Axelson, O., 1998. Diabetes mellitus associated with arsenic exposure in Bangladesh. Am. J. Epidemiol. 148, 198–203.

Rooney, A.A., Boyles, A.L., Wolfe, M.S., Bucher, J.R., Thayer, K.A., 2014. Systematic review and evidence integration for literature-based environmental health science assessments. Environ. Health Perspect. 122, 711–718.

Roy, R.V., Son, Y.O., Pratheeshkumar, P., Wang, L., Hitron, J.A., Divya, S.P., et al., 2015. Epigenetic targets of arsenic: emphasis on epigenetic modifications during carcinogenesis. J. Environ. Pathol. Toxicol. Oncol. 34 (1), 63–84.

Sanders, A.P., Messier, K.P., Shehee, M., Rudo, K., Serre, M.L., Fry, R.C., 2012. Arsenic in North Carolina: public health implications. Environ. Int. 38, 10–16.

Sanders, A.P., Desrosiers, T.A., Warren, J.L., Herring, A.H., Enright, D., Olshan, A.F., et al., 2014. Association between arsenic, cadmium, manganese, and lead levels in private wells and birth defects prevalence in North Carolina: a semi-ecologic study. BMC Public Health 14, 955.

Steinmaus, C., Yuan, Y., Bates, M.N., Smith, A.H., 2003. Case–control study of bladder cancer and drinking water arsenic in the western United States. Am. J. Epidemiol. 158, 1193–1201.

Su, C.C., Lin, Y.Y., Chang, T.K., Chiang, C.T., Chung, J.A., Hsu, Y.Y., et al., 2010. Incidence of oral cancer in relation to nickel and arsenic concentrations in farm soils of patients' residential areas in Taiwan. BMC Public Health 10, 67.

Takahashi, W., Pfenninger, K., Wong, L., 1983. Urinary arsenic, chromium, and copper levels in workers exposed to arsenic-based wood preservatives. Arch. Environ. Health 38, 209–214.

Thomas, K., Pellizzari, E., Berry, M., 1999. Population-based dietary intakes and tap water concentrations for selected elements in the EPA region V national human exposure assessment survey (NHEXAS). J. Expo. Anal. Environ. Epidemiol. 9, 402–413.

Tsai, S.M., Wang, T.N., Ko, Y.C., 1999. Mortality for certain diseases in areas with high levels of arsenic in drinking water. Arch. Environ. Health 54, 186–193.

Tsai, S.Y., Chou, H.Y., HW, T., Chen, C.M., Chen, C.J., 2003. The effects of chronic arsenic exposure from drinking water on the neurobehavioral development in adolescence. Neurotoxicology 24, 747–753.

Tsuji, J.S., Alexander, D.D., Perez, V., Mink, P.J., 2014a. Arsenic exposure and bladder cancer: quantitative assessment of studies in human populations to detect risks at low doses. Toxicology 317, 17–30.

Tsuji, J.S., Perez, V., Garry, M.R., Alexander, D.D., 2014b. Association of low-level arsenic exposure in drinking water with cardiovascular disease: a systematic review and risk assessment. Toxicology 323, 78–94.

Tyrrell, J., Melzer, D., Henley, W., Galloway, T.S., Osborne, N.J., 2013. Associations between socioeconomic status and environmental toxicant concentrations in adults in the USA: NHANES 2001–2010. Environ. Int. 59, 328–335.

U.S. EPA (United States Environmental Protection Agency), 2001. National Primary Drinking Water Regulations; Arsenic and Clarifications to Compliance and New Source Contaminant Monitoring. Federal Register Notice (66 FR 6976). 91. U.S. EPA.

U.S. EPA (United States Environmental Protection Agency), 2005. Guidelines for Carcinogen Risk Assessment.

U.S. EPA (United States Environmental Protection Agency), 2013. Draft Technical Guidance for Assessing Environmental Justice in Regulatory Analysis.

U.S. EPA (United States Environmental Protection Agency), 2013. Integrated Science Assessment of Ozone and Related Photochemical Oxidants (Final Report).

Vinikoor-Imler, L.C., Owens, E.O., Nichols, J.L., Ross, M., Brown, J.S., Sacks, J.D., 2014. Evaluating potential response-modifying factors for associations between ozone and health outcomes: a weight-of-evidence approach. Environ. Health Perspect. 122, 1166.

Vogt, R., Bennett, D., Cassady, D., Frost, J., Ritz, B., Hertz-Picciotto, I., 2012. Cancer and non-cancer health effects from food contaminant exposures for children and adults in California: a risk assessment. Environ. Heal.

Walker, M., Benson, M., Shaw, W.D., 2005. Significance of private water supply wells in a rural Nevada area as a route of exposure to aqueous arsenic. J. Water Health 3, 305–312.

Wei, Y., Zhu, J., Nguyen, A., 2013. Rice Consumption and Urinary Concentrations of Arsenic in us Adults Int. J. Environ. Health Res.

Yang, C.Y., Chiu, H.F., Wu, T.N., Chuang, H.Y., Ho, S.C., 2004. Reduction in kidney cancer mortality following installation of a tap water supply system in an arsenic-endemic area of Taiwan. Arch. Environ. Health 59, 484–488.

Yuan, Y., Marshall, G., Ferreccio, C., Steinmaus, C., Selvin, S., Liaw, J., et al., 2007. Acute myocardial infarction mortality in comparison with lung and bladder cancer mortality in arsenic-exposed region ii of Chile from 1950 to 2000. Am. J. Epidemiol. 166, 1381–1391.

Supplement 1: Search strings used in literature search of in PubMed, Web of Science and ToxNet databases.

Database	Search Strings
PubMed	(arsenic OR "7440-38-2" OR "inorganic arsenic" OR "monomethylarsenic" OR "dimethylarsenic" OR "methylarsenic" OR "monomethylarsonic acid" OR "124-58-3" OR "monomethylarsonous acid" OR "dimethylarsinic acid" OR "75-60-5" OR "dimethylarsinous acid" OR "arsenate" OR "arsenite" OR "cacodylic acid" NOT "arsenic trioxide")
Web of Science	((TS=arsenic OR TS="7440-38-2" OR TS="inorganic arsenic" OR TS=monomethylarsenic OR TS=dimethylarsenic OR TS=methylarsenic OR TS="monomethylarsonic acid" OR TS="124-58-3" OR TS="monomethylarsonous acid" OR TS="dimethylarsinic acid" OR TS="cacodylic acid" OR TS="75-60-5" OR TS="dimethylarsinous acid" OR TS=arsenate OR TS=arsenite OR TS="7784-46-5") NOT TS="arsenic trioxide" NOT WC="Geochemistry Geophysics" NOT WC="Physics Applied" NOT WC="Physics Condensed Matter" NOT WC="Materials Science Coatings Films" NOT WC=Optics NOT WC="Chemistry Physical" NOT WC=Mechanics NOT WC="Instruments Instrumentation" NOT WC="Engineering Manufacturing" NOT WC="Materials Science Characterization Testing" NOT WC=Electrochemistry NOT WC="Metallurgy Metallurgical Engineering" NOT WC="Chemistry Analytical" NOT WC="Engineering Environmental" NOT WC="Materials Science Multidisciplinary" NOT WC="Chemistry Inorganic Nuclear" NOT WC="Engineering Electrical Electronic" NOT WC="Engineering Chemical" NOT WC=Spectroscopy NOT WC=Crystallography NOT WC="Engineering Civil" NOT WC="Nanoscience Nanotechnology" NOT WC=Mineralogy NOT WC="Physics Atomic Molecular Chemical" NOT WC="Mining Mineral Processing" NOT WC="Energy Fuels" NOT WC="Materials Science Paper Wood" NOT WC="Materials Science Ceramics" NOT WC="Materials Science Characterization Testing" NOT WC="Physics Nuclear" NOT WC="Polymer Science" NOT WC=Geology NOT WC=Limnology NOT WC="Engineering Manufacturing" NOT WC="Agricultural Engineering" NOT WC="Engineering Mechanical" NOT WC="Computer Science Hardware Architecture" NOT WC="Imaging Science Photographic Technology")
ToxNet (CASRNs)	@AND+@OR+(@TERM+@rn+7440-38-2+@TERM+@rn+124-58-3+@TERM+@rn+75-60-5+@TERM+@rn+7784-46-5)+@NOT+"arsenic+trioxide"+@NOT+@org+"nih+reporter"
ToxNet (Synonyms)	@AND+@OR+(arsenic+"inorganic+arsenic"+monomethylarsenic+dimethylarsenic+methyl arsenic+"monomethylarsonic+acid"+"monomethylarsonous+acid"+"dimethylarsinic+acid"+ "dimethylarsinous+acid"+arsenate+arsenite+arsenicals+@NOT+"arsenic+trioxide"+@NOT +@org+"nih+reporter"

Supplement 2: Terms used to identify studies relevant to minority, low-income, or indigenous populations

disparities	ethnic group
socioeconomic	ethnic groups
socioeconomics	justice
sociodemographic	injustice
sociodemographics	inequality
sociocultural	inequalities
social class	inequity
social classes	inequities
disenfranchised	inequitable
disadvantaged	racial
underprivileged	racism
underserved	minority
marginalized	minorities
vulnerable	impoverished
population group	poverty
population groups	low income

Joca et al. - Supplementary Figure 5 – PRISMA Checklist

Section	PRISMA Checklist item	Reported on page number	Author Comments
Title			
Title	Identify the report as a systematic review, meta-analysis, or both.	1	Title indicates that manuscript is a systematic review. We did not do a meta-analysis.
Abstract			
Structured summary	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2	Abstract includes information on background, objectives, data sources (i.e., peer reviewed literature), study eligibility criteria, study appraisal and synthesis methods, results, limitations, and conclusions. Participant and intervention information is outside the scope of this review, as it is focused on environmental exposure rather than human clinical trials. The manuscript does not have a systematic review registration number.
Introduction			
Rationale	Describe the rationale for the review in the context of what is already known.	2-3	The introduction captures that despite the revised arsenic standard, exposure above the MCL may still occur. Differential exposure is a key consideration for determining environmental justice implications of chemical exposure.
Objectives	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3	Introduction includes statement indicating that the systematic review is identifying and evaluating evidence of differential arsenic exposure (exposure) in low-income, minority, and indigenous US populations (populations), compared to groups not considered populations of concern (comparison). This review considers environmental chemical exposure, so "exposures" were considered rather than "interventions." Similarly, "populations" were identified rather than "participants."
Methods			
Protocol and registration	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a	A review protocol, registration information, and registration number do not exist for this review. However, the risk of bias evaluation adapted the OHAT method as outlined in the methods section. The evidence integration approach was adapted from the U.S. EPA framework used for the Integrated Science Assessments, as described in the methods section.

Eligibility criteria	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4 and Supplement 2	Section 2.1 Describes the literature search strategy, including the key terms considered. Studies had to be US populations and include at least one of the key terms for EJ. The rationale for selecting key terms is also described. The EJ key terms are provided in Supplement 2.
Information sources	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3	Section 2.1 indicates that PubMed, Web of Science, and ToxNet databases were searched from November 2013, with periodic updates through December 2014.
Search	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplement Figure 1	Supplement 1 includes the search strings used for PubMed, Web of Science, and ToxNet
Study selection	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4 and Figure 1	Section 2.2 describes study selection. Figure 1 outlines the study selection process described in Section 2.2. Exclusion criteria and inclusion criteria are described.
Data collection process	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6 and Table 2	We did not perform a meta-analysis, so data extraction was not necessary for our qualitative evaluation. In response to reviewer comments and to clarify how studies were considered, we present key study details in Table 2. Data extraction is described in Section 2.4.
Data items	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6 and Table 2	Section 2.4 describes the types of data examined, including measures of iAs and selected results. For measures of arsenic exposure, Table 2 includes the species of arsenic and, if available, recorded levels of iAs found in biomarkers such as urine, toenails, or hair. For environmental exposure studies, the results information included levels of inorganic arsenic in water and soil. Where available, demographic characteristics were recorded. Selected findings were considered informative for evaluating evidence of differential iAs exposure
Risk of bias on individual studies	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4-5 and Figure 2	Section 2.3 describes the risk of bias evaluation for individual studies. The OHAT approach was used to evaluate risk of bias. OHAT questions specific for experimental animal or controlled human exposure studies were not evaluated because the literature search was limited to human studies and no controlled human exposure studies were identified. Criteria used to evaluate each OHAT risk of bias question are provided in Figure 2.

Summary measures	State the principal summary measures (e.g., risk ratio, difference in means).	Table 2	Table 2 provides the selected findings of each study, as well as the measurements of iAs and demographics information
Synthesis of results	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n/a	We did not perform a meta-analysis or quantitatively combine study data.
Risk of bias across studies	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a	We did not evaluate risk of bias across studies, but used the individual risk of bias evaluations to inform conclusions based on the cumulative evidence. We did not evaluate publication bias, but the risk of bias evaluation indicated that exposure characterization was the largest data gap.
Additional analyses	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a	We did not perform a meta-analysis or additional quantitative analysis on the data.
Results			
Study selection	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4 and Figure 1	Figure 1 is a flow-diagram indicating the number of studies identified in the initial "general" search and the process to identify studies for this review. The number of studies excluded, as well as the reasons for exclusion, are provided in Figure 1, as well as in Section 2.2.
Study characteristics	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 2	Table 2 summarizes the data extracted from the identified studies.
Risk of bias within studies	Present data on risk of bias of each study and, if available, any outcome level assessment	Table 1 and Supplement 3	Table 1 summarizes the risk of bias evaluations for each individual study. For each individual study, Supplement 3 provides the rationale for risk of bias rankings for the 10 OHAT questions.
Results of individual studies	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7-9 and Table 2	The results of individual studies specific to this systematic review are summarized in Section 3.2 and in Table 2. This review focused on environmental exposures, so interventions were not applicable. Similarly, the health effects associated with exposure were not evaluated in this review; therefore, effect estimates were not applicable.
Synthesis of results	Present results of each meta-analysis done, including confidence intervals and measures of consistency	n/a	We did not do a meta-analysis.

Risk of bias across studies	Present results of any assessment of risk of bias across studies	n/a	We did not do a risk of bias evaluation across the body of evidence; however, we used risk of bias evaluations from individual studies to identify data gaps and inform our conclusions.
Additional analysis	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression).	n/a	We did not do an additional quantitative analyses of the data.
Discussion			
Summary of evidence	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-11	Section 4.1 summarizes the main findings of the studies, drawing overall conclusions and identifying data gaps.
Limitations	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-12	Section 4.2 describes the limitations in the study, including the literature search, lack of direct iAs measurements, and incomplete demographic information.
Conclusions	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12	Section 4.3 summarizes the overall conclusions of the manuscript.
Funding			
Funding	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13	Section 5 provides the funding support information for the authors.